SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Non-Drowsy Sinutab

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Non-drowsy Sinutab tablets contain 30mg EP Pseudoephedrine Hydrochloride and 500mg Paracetamol Ph Eur.

3 PHARMACEUTICAL FORM

Tablets

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Non-Drowsy Sinutab is indicated for the symptomatic relief of conditions where congestion of the mucous membranes of the upper respiratory tract, especially nasal mucosa and sinuses, is accompanied by mild to moderate pain or pyrexia, e.g.: the common cold and influenza, sinusitis, nasopharyngitis, allergic rhinitis and vasomotor rhinitis.

4.2 Posology and method of administration

Posology

Adults and children aged 16 years and over:
Two tablets every four to six hours, up to four times a day. Maximum daily dose: 8 tablets (i.e. 240 mg pseudoephedrine hydrochloride, 4 g paracetamol).

Children aged 12 years to 15 years
One tablet every four to six hours, up to four times a day. Maximum daily dose: 4 tablets (i.e. 120 mg pseudoephedrine hydrochloride, 2 g paracetamol).

Children under 12 years:
NON-DROWSY SINUTAB is contraindicated in children under the age of 12 years (see section 4.3).

The Elderly:
There have been no specific studies of NON-DROWSY SINUTAB in the elderly. Experience has indicated that normal adult dosage is appropriate.

In the elderly the rate and extent of paracetamol absorption is normal but plasma half life is longer and paracetamol clearance is lower than in young adults.

Hepatic dysfunction
Caution should be exercised when administering NON-DROWSY SINUTAB to patients with severe hepatic impairment.

Renal dysfunction:
Caution should be exercised when administering NON-DROWSY SINUTAB to patients with moderate renal impairment.

Method of administration
For oral use

4.3 Contraindications

NON-DROWSY SINUTAB is contraindicated in individuals with known hypersensitivity to paracetamol, pseudoephedrine or any of the excipients listed in section 6.1.

Concomitant use of other sympathomimetic decongestants, beta-blockers or monoamine oxidase inhibitors (MAOIs), or within 14 days of stopping MAOI treatment (see section 4.5). The concomitant use of MAOIs may cause a rise in blood pressure and/or hypertensive crisis.

Cardiovascular disease including hypertension
Diabetes mellitus
Phaeochromocytoma
Hyperthyroidism
Closed angle glaucoma
Severe acute or chronic kidney disease/renal failure

Not to be used in children under the age of 12 years.

4.4 Special warnings and precautions for use

Patients experiencing difficulty in urination and/or enlargement of the prostate, or patients with thyroid disease who are receiving thyroid hormones should not take pseudoephedrine unless directed by a physician.

Caution should be exercised when using the product in the presence of severe hepatic impairment or moderate to severe renal impairment (particularly if accompanied by cardiovascular disease), or in occlusive vascular disease. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.

If any of the following occur, this product should be stopped:
- Hallucinations

- Restlessness
- Sleep disturbances

Severe Skin reactions: Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of this medicine should be discontinued, and appropriate measures taken if needed.

Ischaemic colitis: Some cases of ischaemic colitis have been reported with pseudoephedrine. Pseudoephedrine should be discontinued, and medical advice sought if sudden abdominal pain, rectal bleeding or other symptoms of ischaemic colitis develop.

Ischaemic optic neuropathy: Cases of ischaemic optic neuropathy have been reported with pseudoephedrine. Pseudoephedrine should be discontinued if sudden loss of vision or decreased visual acuity such as scotoma occurs.

Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS)
Cases of PRES and RCVS have been reported with the use of pseudoephedrine-containing products (see section 4.8). The risk is increased in patients with severe or uncontrolled hypertension, or with severe acute or chronic kidney disease/renal failure (see section 4.3).
Pseudoephedrine should be discontinued and immediate medical assistance sought if the following symptoms occur: sudden severe headache or thunderclap headache, nausea, vomiting, confusion, seizures and/or visual disturbances.
Most reported cases of PRES and RCVS resolved following discontinuation and appropriate treatment.

Taking this product with other paracetamol-containing products, could lead to overdose and should therefore be avoided.

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism), who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring, is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

Risks of abuse

Pseudoephedrine carries the risk of abuse. Increased doses may ultimately produce toxicity. Continuous use can lead to tolerance resulting in an increased risk of overdosing. The recommended maximum dose and treatment duration should not be exceeded (see section 4.2).

4.5 Interaction with other medicinal products and other forms of interaction

MAOIs (see section 4.3) and/or RIMAs: Pseudoephedrine exerts its vasoconstricting properties by stimulating α-adrenergic receptors and displacing noradrenaline from neuronal storage sites. Since monoamine oxidase inhibitors (MAOIs) impede the metabolism of sympathomimetic amines and increase the store of releasable noradrenaline in adrenergic nerve endings, MAOIs may potentiate the pressor effect of pseudoephedrine. This product should not be used in patients taking monoamine inhibitors or within 14 days of stopping treatment as there is a risk of hypertensive crisis.

Moclobemide: Risk of hypertensive crisis

Sympathomimetic agents: Concomitant use of this product with tricyclic antidepressants or sympathomimetic agents (such as decongestants, appetite suppressants and amphetamine-like psychostimulants) or with monoamine oxidase inhibitors may cause a rise in blood pressure.

Antihypertensives: Because of the pseudoephedrine content, this product may partially reverse the hypotensive action of antihypertensive drugs which interfere with sympathetic activity including bretylium, betanidine, guanethedine, debrisoquine, methyldopa, adrenergic neurone blockers and beta-blockers.

Cardiac glycosides: Increased risk of dysrhythmias.

Ergot alkaloids (ergotamine & methysergide): Increased risk of ergotism

Oxytocin: Risk of hypertension

Anticholinergic drugs: Enhances effects of anticholinergic drugs (such as tricyclic antidepressants)

Anaesthetic agents: Concurrent use with halogenated anaesthetic agents such as chloroform, cyclopropane, halothane, enflurane or isoflurane may provoke or worsen ventricular arrhythmias.

Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual's ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

The use of drugs which induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptive steroids, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of the drug and a faster elimination rate.

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and absorption reduced by cholestyramine.

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risks factors (see section 4.4).

4.6 Fertility, pregnancy and lactation

There are no adequate and well-controlled clinical studies in pregnant or breast-feeding women for the combination of paracetamol and pseudoephedrine.

This product should not be used during pregnancy or lactation unless the potential benefit of treatment to the mother outweighs the possible risks to the developing foetus or breastfeeding infant.

Pregnancy

The safety of pseudoephedrine in pregnancy has not been established.

A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

Breastfeeding

Pseudoephedrine is excreted in breast milk in small amounts but the effect of this on breast-fed infants is not known. It has been estimated that approximately 0.4 to 0.7% of a single 60 mg dose of pseudoephedrine ingested by a nursing mother will be excreted in the breast milk over 24 hours. Data from a study of lactating mothers taking 60 mg pseudoephedrine every 6 hours suggests that from 2.2 to 6.7% of the maximum daily dose (240 mg) may be available to the infant from a breastfeeding mother.

Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast feeding. A pharmacokinetic study of paracetamol in 12 nursing mothers revealed that less than 1% of a 650 mg oral dose of paracetamol appeared in the breast milk. Similar findings have been reported in other

studies, therefore maternal ingestion of therapeutic doses of paracetamol does not appear to present a risk to the infant.

Fertility

No studies have been conducted in animals to determine whether pseudoephedrine has the potential to impair fertility. There is no information of the effect of NON-DROWSY SINUTAB on fertility.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Adverse drug reactions identified during clinical trials and post-marketing experience with paracetamol, pseudoephedrine, or the combination are listed below by System Organ Class (SOC).

The frequencies are defined according to the following convention:
Very common ≥1/10
Common ≥1/100 and < 1/10
Uncommon ≥1/1,000 and <1/100
Rare ≥1/10,000 and <1/1,000
Very rare <1/10,000, including isolated reports
Not known (cannot be estimated from the available data)

ADRs are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available, or 2) when incidence cannot be estimated, frequency category is listed as 'Not known'.

System Organ Class (SOC)	**Frequency**	**Adverse Drug Reaction (Preferred Term)**
Blood and lymphatic system disorders	Not known	Blood disorders, blood dyscrasias (including agranulocytosis and thrombocytopenia) have been reported following paracetamol use but were not necessarily causally related to the drug
Immune system disorders	Rare	Hypersensitivity (cross-sensitivity may occur with other sympathomimetics)
Psychiatric disorders	Common	Insomnia Nervousness

	Not known	Anxiety Euphoric mood Excitability Hallucinations Irritability Paranoid delusions Restlessness Sleep disorder
Nervous system disorders	Very common	Headache
	Common	Dizziness
	Not known	Cerebrovascular accident Paraesthesia Posterior reversible encephalopathy syndrome (PRES) (see section 4.4) Reversible cerebral vasoconstriction syndrome (RCVS) (see section 4.4) Psychomotor hyperactivity Somnolence Tremor
Eye Disorders	Not known	Ischaemic optic neuropathy
Cardiac disorders	Not known	Dysrhythmias Myocardial infarction/myocardial ischaemia Palpitations Tachycardia
Vascular disorders	Not known	Hypertension
Gastrointestinal disorders	Common	Dry mouth Nausea
	Not known	Abdominal pain Diarrhoea Ischaemic colitis Vomiting
Hepatobiliary disorders	Rare	Hepatic necrosis
Skin and subcutaneous tissue disorders	Rare	Rash
	Not known	Angioedema Fixed eruption

		Pruritus Rash pruritic Severe skin reactions, including Acute generalised exanthematous pustulosis (AGEP) Urticaria
Renal and urinary disorders	Uncommon	Nephropathy toxic
	Not known	Dysuria Renal papillary necrosis (after prolonged administration) Urinary retention (in men whom prostatic enlargement could have been an important predisposing factor)
Metabolism and nutrition disorders	Not known	High anion gap metabolic acidosis

Chronic hepatic necrosis has been reported in a patient who took daily therapeutic dosages of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of their disease improved after paracetamol withdrawal.

Very rare cases of serious skin reactions have been reported with paracetamol.

High anion gap metabolic acidosis
Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Signs and symptoms

Paracetamol

Liver damage is possible in adults who have taken 10 g or more of paracetamol. Ingestion of 5 g or more of paracetamol may lead to liver damage if the patient has risk factors (see below).

Risk Factors:

If the patient

A. Is on long term treatment with carbamazepine, phenobarbital, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.

Or

B. Regularly consumes ethanol in excess of recommended amounts.

Or

C. Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema, coma and death.

Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Haemolytic anaemia (in patients with glucose-6-phosphate dehydrogenase [G6PD] deficiency): Haemolysis has been reported in patients with G6PD deficiency, with use of paracetamol in overdose.

Management

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is

not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

Pseudoephedrine

Symptoms

Overdose may result in:

Hyperglycaemia, hypokalaemia, CNS stimulation, insomnia; irritability, restlessness, anxiety, agitation; confusion, delirium, hallucinations, psychoses, seizures, tremor, intracranial haemorrhage including intracerebral haemorrhage, drowsiness in children, mydriasis, palpitations, tachycardia, reflex bradycardia, supraventricular and ventricular arrhythmias, dysrhythmias, myocardial infarction, hypertension, vomiting, ischaemic bowel infarction, acute renal failure, difficulty in micturition.

Management

Necessary measures should be taken to maintain and support respiration and control convulsions. Catheterisation of the bladder may be necessary. If desired, the elimination of pseudoephedrine can be accelerated by acid diuresis or by dialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Expectorants, ATC code: N02B E51

Pseudoephedrine
Pseudoephedrine has direct and indirect sympathomimetic activity and is an orally effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation of systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.

Paracetamol
Paracetamol has analgesic and antipyretic actions but only weak anti-inflammatory properties. This may be explained by presence of cellular peroxides at sites of inflammation which prevent inhibition of cyclo-oxygenase by paracetamol. At other sites associated with low levels of cellular perioxides, e.g. pain, fever, paracetamol can successfully inhibit prostaglandin biosynthesis.

5.2 Pharmacokinetic properties

Pseudoephedrine

Pseudoephedrine is partly metabolised in the liver by N-demethylation to norpseudoephedrine, an active metabolite. Pseudoephedrine and its metabolite are excreted in the urine: 55% to 75% of a dose is excreted unchanged. The rate of urinary excretion of pseudoephedrine is accelerated when the urine is acidified. Conversely as the urine pH increases, the rate of urinary excretion is slowed.

Paracetamol
Peak plasma paracetamol concentration usually occurs between 30 and 90 minutes after oral ingestion. Paracetamol is distributed uniformly throughout most body fluids and is only 15 to 25 per cent bound to plasma proteins. The plasma half life of paracetamol after therapeutic doses is in the range of 1 to 3 hours.

5.3 Preclinical safety data

The active ingredients of NON-DROWSY SINUTAB are well known constituents of medicinal products and their safety profile is well documented. The results of pre-clinical studies do not add anything of relevance for therapeutic purposes.

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available for paracetamol.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

(Contained in compressible Paracetamol 90%)
Pregelatinised Maize Starch
Crospovidone
Povidone K30
Stearic Acid

Other ingredients
Microcrystalline Cellulose
Sodium Starch Glycollate
Magnesium Stearate

6.2 Incompatibilities

None known

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 25ºC

Store in the original packaging

6.5 Nature and contents of container

Carton containing 4, 12, 15 or 24 tablets.

Each blister strip consists of a white, opaque PVC/PVdC film and paper/aluminium foil child resistant blister lidding.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

McNeil Products Limited
50 – 100 Holmers Farm Way
High Wycombe
Buckinghamshire
HP12 4EG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 15513/0027

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/03/1997 / 23/02/2011

10 DATE OF REVISION OF THE TEXT

18/05/2025